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which upon activation has substantially the same biological activity for blood coagulation as Factor VIIa, the joined sequences being followed downstream by a polyadenylation signal.

23. (Amended) The cells of claim 16 wherein said plasmid [includes] comprises a promoter followed downstream by [a set of RNA splice sites, said RNA splice sites being followed downstream by] a first nucleotide sequence derived from a genomic clone of Factor VII, joined to a second nucleotide sequence positioned downstream of said first sequence, said second sequence derived from a cDNA clone of Factor VII, the joined sequences coding for a protein which upon activation has substantially the same biological activity for blood coagulation as Factor VIIa, the joined sequences being followed downstream by a polyadenylation signal.

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27. (Amended) The method of claim 24 wherein [at least a portion of] said DNA sequence comprises [is derived from a] Factor VII cDNA [clone of Factor VII].

28. (Amended) The method of claim 24 wherein [at least a portion of] said DNA sequence comprises [is derived from a] Factor VII genomic DNA [clone of Factor VII].

REMARKS

Reconsideration of the application in view of the above amendments and the following remarks is requested.

Claims 1-32 are now in this application. Claims 11-16, 19-23, and 27-28 have been amended.

Applicants note that the Examiner has provisionally rejected claims 1-32 under the doctrine of obviousness-type double patenting, as being unpatentable over claims 1-44 and 46-48 of co-pending application Serial No. 724,311. Although this is only a provisional obviousness-type double patenting

rejection, as discussed during the interview with the Examiner on April 21, 1987, applicants have submitted herewith an appropriate terminal disclaimer, and thereby overcome the double patenting rejection based upon Serial No. 724,311.

The Examiner rejected claims 16 and 17 under 35 U.S.C. § 101, because the Examiner believes the claims are broadly drawn to the cells of a liver and as such are drawn to a natural product. As discussed with the Examiner during the interview, applicants have amended claim 16 to recite that the cells "produce Factor VII in recoverable amounts." In addition, the claim as submitted recited that the cells are "stably transfected with a recombinant plasmid," a condition resulting from human intervention. Therefore, applicants believe that the rejection of claim 16 under §101 has been overcome. Since claim 17 depends from and contains all the limitations of claim 16 as amended, applicants believe that claim 17 overcomes the §101 rejection in a similar manner.

The Examiner objected to the specification under 35 U.S.C. § 112 as failing to provide an adequate description of the invention and failing to provide an enabling disclosure. In particular, although a deposit had been made in the application as filed, the Examiner believed it was not clear if the deposit met all of the criteria set forth in MPEP 608.101(p)(C). In order to fully meet all of these criteria, applicants have provided herewith a declaration avering that: (a) during the pendency of the application, access to the deposit will be afforded to the Commissioner upon request; (b) that all restrictions upon availability to the public will be irrevocably removed upon granting of the patent; (c) that the deposit will be maintained in a public depository for a period of thirty (30) years or five years after the last request, or for the effective life of the patent, whichever is longer; and (d) that the deposit will be replaced if it should ever become inviable. Therefore, applicants believe that the rejection of the claims based upon the objection to the specification under 35 U.S.C. § 112 has been overcome.

However, applicants believe that these deposits are not necessary in order to practice the present invention. More specifically, the examples as written provide a description of the invention in sufficient detail so as to allow one of ordinary skill in the art to obtain cDNA or genomic clones encoding Factor VII or another protein having, upon activation, substantially the same biological activity for blood coagulation as Factor VIIa. The disclosed processes are within the level of ordinary skill in the art and are sufficiently reproducible to avoid the need to deposit biological materials. Through use of the DNA and amino acid sequence information provided within the application, and by following the procedures described in the examples, one of ordinary skill in the art could prepare the necessary clones, insert them into expression vectors, transfect selected cell lines, and express the proteins of the present invention. Methods of performing each essential step in this process are disclosed in sufficient detail to permit such an individual to readily reproduce the invention. Furthermore, in many instances alternative methods are well known in the art, and may be substituted at the discretion of the practitioner to produce equivalent results. The necessary starting materials may be prepared as disclosed, or may be obtained from commercial sources or from other sources readily available to those skilled in the art. In addition, it will be apparent to one skilled in the art that in many instances the selection of a particular cloning vehicle or other material is a matter of convenience and individual discretion, which substitution is possible without materially affecting the focus of the present invention. While applicants have deposited certain materials in accordance with the present invention, these deposits merely represent certain preferred embodiments of the present invention. The use of deposited vectors is not necessary for the practice of the present invention, but is merely provided as a convenience. While deposits were made under the terms of the Budapest treaty and therefore, along with the declaration submitted herewith, satisfy the

requirements of MPEP 608.01(b)(C), it is believed that such deposits are not necessary to practice the present invention.

Claims 2, 3, 6, 7, 11, 12, 14, 15, 19, 20, 22, 23, 27, 28, 31 and 32 were rejected as being indefinite in the recitation of "derived from," as the Examiner did not believe it was clear if a chemical modification or mere isolation was intended. As discussed with the Examiner, the phrase "derived from" is intended to include both chemical modifications and mere isolations. For example, such chemical modifications would include elimination of introns from genomic DNA and enzymatic cleavage of fragment ends and subsequent ligation. It would also be apparent to one skilled in the art that "derived from" would include a variety of physical manipulations needed to construct the claimed compositions. Many such manipulations are exemplified within the disclosure, including oligonucleotide-directed mutagenesis to join sequences in the correct reading frame, and restriction endonuclease digestion and ligation. Therefore, applicants believe that use of the phrase "derived from" is entirely acceptable and is not indefinite. Applicants wish to point out that in certain instances, for matters of convenience, the phrase "is derived from" has been removed, for instance in claims 11, 12, 19, 20, and 27-28, although no change in the intended scope of the claim as submitted is contemplated.

The Examiner also rejected claims 13-15 and 21-23 as being indefinite in the recitation of "includes" or "including," as the Examiner did not believe it was clear if open or closed language was intended. As discussed with the Examiner during the interview, applicants have amended claims 13-15 and 21-23 to recite the term "comprising," and have removed the terms "including" and "includes." This amendment is not intended to affect the scope of the claims as submitted, but confirms that "open" language was intended.

Claims 13-15 and 21-23 were also rejected as being indefinite in the recitation of "RNA splice sites." As discussed with the Examiner, the use of the phrase "RNA splice

sites" is not essential to claims 13-15 and 21-23, and therefore has been removed.

The Examiner also rejected claims 11, 12, 19, 20, 27 and 28 as being indefinite in the recitation of "at least a portion of." As discussed with the Examiner during the interview, applicants believe that this objection is valid only where the claims are not limited by a statement of function. The present claims contain such a limitation in that the DNA sequence must encode Factor VII. There has never been a requirement that claims, particularly dependent claims, are read in a vacuum or that they be operative in every possible combination. While it may be true that the phrase "at least a portion of" could be literally read to encompass a single nucleotide, those skilled in the art cannot be expected to understand these terms as including proportions, combinations or possibilities that would be ineffective to produce the desired results, i.e., a protein having the biological activity of Factor VII. On the contrary, it would be more than reasonably evident to those skilled in the art which "portions" would be suitable for use within the present invention, given the limitations set forth above. However, without intending to change the scope of the claims, applicants have amended claims 11, 12, 19, 20, 27 and 28 to recite that the DNA sequence comprises either Factor VII cDNA or Factor VII genomic DNA. Therefore, applicants believe that they have overcome the rejection of these claims as being indefinite.

On the basis of the above amendments and remarks, reconsideration of the application and its allowance are requested.

Respectfully submitted,
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SEED and BERRY



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Enclosures: Declaration
Terminal disclaimer
Extension of Time